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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/647,054 | 02/06/2001 | Peter Joseph Cassidy | 707.025US1 | 3789 |

21186 7590 02/19/2010

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| EXAMINER | |
|---|---|
| GROSS, CHRISTOPHER M | |
| ART UNIT | PAPER NUMBER |
| 1639 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 02/19/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@slwip.com
request@slwip.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/647,054 | CASSIDY ET AL. | |
| | Examiner | Art Unit | |
| | CHRISTOPHER M. GROSS | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *113-144* is/are pending in the application.

4a) Of the above claim(s) *114-118,122-123,125,127-133,136,139,141-144* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *113,119-121,124,126,134,135,137,138 and 140* is/are rejected.

7)☒ Claim(s) *113 and 136* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Responsive to communications entered 10/20/2009. Claims 113-144 are pending. Claims 114-118,122-123,125,127-133,136,139,141-144 are withdrawn. Claims 113, 119, 120, 121, 124, 126, 134, 135, 137, 138 and 140 are under consideration.

### *Priority*

This application is a 371 of PCT/AU99/00207 03/24/1999 which claims priority to AUSTRALIA patent PP2548 03/24/1998. The acceptance notice from DO/EO mailed 11/1/2006 is in the file.

### *Maintained Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 113, 119, 120, 121, 124, 126,134,135, 137, 138 and 140 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Ma et al** (1995 Protein Peptide Letters 2:347-350; PTO 892 4/5/2006) in view of **Tsunoda et al** (1996 Tetrahedron Letters 37:2457-2458; PTO 892 1/10/2007) **or Tsunoda et al II** (1993 Tetrahedron Letters 34: 1639-1642) as evidenced by the 1/21/2008 Jenkins declaration.

The claimed invention is drawn to a protein gamma turn mimetic, in which the hydrogen bond is replaced by an ethlyene bridge in the form of the Markush group structure illustrated in claim 113, including cyclic 1,4 diazapan-2-ones.

Claims 119, 120, 121, 124, 126,134,135, 137, 138 and 140 constitute variations of said structure.

**Ma et al** teach throughout the publication and especially the target molecule on p 347, the same 1,4 diazapan-2-one mimetic bearing the tripeptide sequence Ile-Ala/Asp-Gly; therein including R groups being amino acid side chains, Z and Z' being H, M', M'', $M^3$, $M^4$ being H, $M^5$ and $M^6$ are taken together with the carbon atom to which they are attached to from a carbonyl group, $R^C$ is the carboxy terminus of the mimetic, $Pg^N$ is shown as Z (a.k.a. Cbz; benzyloxycarbonyl) or Boc in an alternative embodiments in schemes 1 and 2, respectively. Therefore the disclosure of Ma et al reads on claims 113,121,134,135,137 and 138.

Ma et al teach C-terminal protection as an ethyl ester, reading on the protecting group of claim 119 and alkoxy group of claim 120, as well as the protecting group of claims 124,126 and 140.

Evidence provided in the 10/27/2008 Cassidy declaration indicates that the final Mitsunobo reaction (f) in scheme 2 of Ma et al provides a N-Boc aziridine (see compound 3 p 7) rather than the desired 1,4 diazapan-2-one mimetic precursor (see compound 2 p 7).

**Tsunoda et al and Tsunoda et al II** teach, throughout the documents and especially the tables in each, tosyl (Ts) protection of nitrogen rather than Cbz for performing Mitsunobo reactions.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to utilize the Ts protection of Tsunoda et al or

Tsunoda et al II instead of Cbz in step (f) of scheme 2 of Ma et al to prepare the 1,4 diazapan-2-one mimetic.

One of ordinary skill in the art would have been motivated to use utilize the Ts protection of Tsunoda et al or Tsunoda et al II instead of Cbz in step (f) of scheme 2 of Ma et al 1,4 diazapan-2-one mimetic because Tsunoda et al II state "If HA [protected amine] has a pKa larger than 11, the yield of RA [Mitsunobo product] lowers considerably, and with HA having a larger pKa than 13 the desired reaction does not occur" and unlike TsNH, CbzNH has a pKa considerably greater than 11.

One of ordinary skill in the art would have had a reasonable expectation of success in substituting Ts per Tsunoda et al or Tsunoda et al II for Cbz protection of nitrogen per Ma et al in preparing the 1,4 diazapan-2-one mimetic because: (i) all three references concern Mitsunobo chemistry, thus the refinements of Tsunoda et al and Tsunoda et al II are well suited toward Ma et al and (ii) even assuming *arguendo* the Mitsunobo reaction even with tosyl nitrogen protection does not occur - for what ever reason - according to section 12 of applicant's own Jenkins declaration, N-Boc aziridines may nevertheless be opened by acidic sulfonamides (tosyl protected nitrogen) and therein provide the desired 1,4 diazapan-2-one mimetic precursor, albeit through an alternative pathway.

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Please note that the above rejection has been modified from the original version to more clearly address applicants' arguments and comments.

*Response to Arguments*

In the remarks entered 10/20/2009 applicant argues: no motivation exists for the combination and there lacks a reasonable expectation of success.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

On p 9 first full paragraph of the remarks, applicant asserts, there is a lack of motivation to combine the teachings of Ma et al with the Tsunoda references because in attempting to perform the Mitsunobo reaction in the manner of Ma et al, one of skill in the art would not recognize they would need to alter the reaction conditions, since they would assume the reaction would provide the desired 1,4 diazapan-2-one.

In this vein, the following is noted. First, as mentioned in the rejection above, the Tsunoda references teach in order for the Mitsunobo reaction to occur, like TsNH and unlike CbzNH, the pKa of the protected nitrogen must be less than 11. Accordingly the skilled artisan might suspect that the Mitsunobo reaction would not work, thus providing the motivation to use Ts instead of Cbz protection, as advocated by the Tsunoda et al. Second, In accordance with MPEP 716.07, it is to be presumed also that skilled workers would as a matter of course, if they do not immediately obtain desired results, make certain experiments and adaptations, within the skill of the competent worker. *In re Michalek,* 162 F.2d 229, 74 USPQ 107 (CCPA 1947); *In re Reid*, 179 F.2d 998, 84 USPQ 478 (CCPA 1950). Here, skilled workers would as a matter of course, if they do not immediately obtain the desired 1,4 diazapan-2-one, make certain experiments and

adaptations, within the skill of the competent worker, such as changing protecting groups from Cbz to Ts.

On p 9 second and third paragraph of the remarks, applicant argues the Tsunoda references provide evidence that the Mitsunobo reaction of Ma et al is will not occur because, applicant contends, secondary alcohols (like Ma et al) require higher temperatures to react thus, applicant asserts, when reacted with a branched amine (like Ma et al ) the skilled artisan would expect yields to be drastically reduced and furthermore the elevated temperatures of Tsunoda et al would be expected to decompose the Boc protecting group of Ma et al.

In this vein, the following is noted. First, while the examiner acknowledges that secondary alcohols perhaps constitute a less preferred embodiment in the Tsunoda references, the reaction nevertheless proceeds with secondary alcohols: see tables of each Tsunoda reference. Second, the model reactions disclosed in the Tsunoda et al references concern intermolecular reactions whereas the ring closure of Ma et al concerns an intramolecular transformation, thus it is not evident that elevated temperatures would necessarily be required. With regard to branched amines (i.e. amino acids such as alanine of Ma et al), the examiner is not aware of any reduced kinetics such as when performing other types of chemistry such as solid phase peptide synthesis (i.e. alanine is not particularly sterically hindered). Also, applicant's argument is not commensurate with the scope of the claims, which are drawn to $R^2$ being H, such as in glycine, a *non* branched amino acid. Finally assuming *arguendo* that the elevated temperatures of the Tsunoda references is required, which might lead to degradation of

Boc, it is noted that $Pg^N$ is defined in the specification p 10 line 28-29 and claim 121 as part or N-terminal portion or the mimetic, which is broad enough to embrace, for example, the deprotected amine. Alternatively, again assuming *arguendo* that the elevated temperatures of the Tsunoda references is required, which might lead to degradation of Boc, the Boc may be simply re-introduced using reagents such as Boc anhydride upon cooling following the formation of the lactam ring (1,4 diazapan-2-one): again as mentioned above, in accordance with MPEP 716.07, it is to be presumed also that skilled workers would as a matter of course, if they do not immediately obtain desired results, make certain experiments and adaptations, within the skill of the competent worker. *In re Michalek*, 162 F.2d 229, 74 USPQ 107 (CCPA 1947); *In re Reid*, 179 F.2d 998, 84 USPQ 478 (CCPA 1950).

Additionally, in accordance with *In re O 'Farrell,* 853 F.2d 894, 903,907 USPQ2d 1673 (Fed. Cir. 1988) "Obviousness does not require absolute predictability of success." Here, while not necessarily absolute, both Ma et al in view of Tsunoda et al or Tsunoda et al II as well as applicant's own Jenkins declaration each predict a 1,4 diazapan-2-one as the expected product.

Finally, this line of reasoning is not found persuasive because the arguments of counsel cannot take the place of evidence in the record. In re Schulze,346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.") (see MPEP 2145 I.) In the instant case, Applicant's

counsel argues: secondary alcohols plus branched amines will not undergo a Mitsunobo transformation and elevated temperatures will destroy Boc, however counsel does not provide objective evidence establishing these facts.

On p 10, first and second paragraphs of the remarks, first applicant asserts again that the it would not be obvious to replace the Cbz group of Ma et al for the Ts group of the Tsunoda references because the of the overwhelming preference for forming three (aziridines) and five membered ring systems (oxazolines) over seven-membered ring systems (diazapanones), as evidenced by the Jenkins declaration (section 7).

In this regard the following is noted. With regard to formation of oxazolines, there is simply no conclusive evidence on the record that such a compound is formed using the Mitsunobo reaction conditions according to Ma et al, much less Ma et al when using Ts. See Jenkins declaration section 11. With regard to aziridines, the examiner does not deny the possibility that this intermediate may be formed, however in accordance with the section 12 of Jenkins declaration, said aziridines may be subsequently converted to the desired diazapanone the tosylamide anion mediated aziridine ring opening.

Applicant further argues that it is impossible to predict which position the aziridine would be opened, thus 1,4 diazapan-2-one as well as an 8 membered ring side product may form. Again, this line of reasoning is not found persuasive because the arguments of counsel cannot take the place of evidence in the record. In re Schulze,346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) (“An assertion of what seems to follow from

common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.") (see MPEP 2145 I.) In the instant case, Applicant's counsel argues any aziridine formed would be equally likely to form an 8 membered ring, however counsel does not provide objective evidence establishing this fact.

Again, in accordance with *In re O 'Farrell,* 853 F.2d 894, 903,907 USPQ2d 1673 (Fed. Cir. 1988) "Obviousness does not require absolute predictability of success." Here, while not necessarily absolute, both Ma et al in view of Tsunoda et al or Tsunoda et al II as well as applicant's own Jenkins declaration each predict a 1,4 diazapan-2-one as the expected product.

Lastly, for the record, the refinements to Mitsunobo chemistry, from Ito laboratory as disclosed in the Tsunoda references, concerning replacement of Cbz with Ts due to its attractive pKa, in fact, inspired the Lazaro research group to publish two follow up papers to Ma et al. While not prior art, see Nouvet at al 1999 Tetrahedron 55:4685-4698 on p 4687 (IDS entry 5/18/2006) first paragraph and Nouvet et al 1998 Tetrahedron Letters 39:2099-2012 on p 2100 three lines from the bottom.

Claims 113, 119, 120, 121, 124, 126,134,135, 137, 138 and 140 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Ma et al** (1995 Protein Peptide Letters 2:347-350; PTO 892 4/5/2006) in view of **Tsunoda et al** (1996 Tetrahedron Letters 37:2457-2458; PTO 892 1/10/2007) **or Tsunoda et al II (**1993 Tetrahedron

Letters 34: 1639-1642) as evidenced by the 1/21/2008 Jenkins declaration further in view of **Mammi et al** (1985 JACS 107:4008-4013).

**Ma et al in view of Tsunoda et al or Tsunoda et al II** is relied on as above.

Ma et al in view of Tsunoda et al or Tsunoda et al II do not teach a protein gamma turn mimetic with the tripeptide sequence Gly-Phe-Leu.

**Mammi et al** teach, throughout the document and especially the abstract, table II and figure 7, a highly active opioid peptide (enkephalin) analog H-Tyr-c[D-$A_2$bu-Gly-Phe-Leu-] with the sequence Gly-Phe-Leu (elected species) in a gamma turn conformation stabilized by a hydrogen bond between Leu NH and Gly CO.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to generate an enkephalin analog of Mammi et al locked into place with an ethylene bridge in the manner of Ma et al in view of Tsunoda et al or Tsunoda et al II.

One of ordinary skill in the art would have been motivated to generate an enkephalin analog of Mammi et al locked into place with an ethylene bridge in the manner of Ma et al in view of Tsunoda et al or Tsunoda et al II because said hydrogen bond is disrupted by water and analogs with additional restraints are desirable, as noted by Mammi et al in the last sentence of the abstract and conclusions section on p 4013.

One of ordinary skill in the art could incorporate Gly-Phe-Leu locked into a gamma turn conformation with an ethlyene bridge per Ma et al in view of Tsunoda et al or Tsunoda et al II into the enkephalins of Mammi et al because the Boc protection of Gly (provided by Ma et al) is used in Boc based solid phase peptide synthesis, a robust

technique for preparing opioid peptides, such as disclosed by Mammi et al, well recognized in the art.

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Please note that the above rejection has been modified from the original version to more clearly address applicants' arguments and comments.

*Response to Arguments*

In the remarks entered 10/20/2009 applicant argues : no motivation exists for the combination.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

First in the paragraph bridging pp 11-12 of the remarks, applicant argues that it would be more obvious to replace the other (D-$A_2$bu D-$A_2$bu CO or Phe CO) hydrogen bond rather than the Leu NH and Gly CO hydrogen bond because the enkephalin analog of Mammi et al retains high potency when tested in aqueous solution despite disruption of the latter hydrogen bond.

In this vein the following is noted. The 1,4 diazapan-2-one of Ma et al in view of the Tsunoda references constitutes a mimetic for gamma turns such as the Leu NH and Gly CO hydrogen bond. The $A_2$bu D-$A_2$bu CO or Phe CO hydrogen bond, on the other hand constitutes beta type structure. Accordingly, it would be illogical to replace the beta type structure of the D-$A_2$bu D-$A_2$bu CO or Phe CO hydrogen bond with a

gamma turn mimetic, as suggested by applicant. Furthermore, absent evidence to the contrary, precisely because the Leu NH and Gly CO gamma turn is apparently not critical for activity, it would provide a rather innocuous location to make such a modification.

Second, applicant argues in the same passage of the remarks, the lack of obviousness is reflected in the many papers, such as Berezowska et al (2009 Chem. Biol. Drug Des. 74:329-334), published since Mammi which provide a conformational constraint via cyclization.

In this regard it is noted the H-Tyr-c[D-$A_2$bu-Gly-Phe-Leu-] enkephalin analog of Mammi *already is cyclic,* nevertheless, as Mammi et al disclose on p 4011 right column first paragraph under 'Discussion' the compound is *not* rigid. Accordingly cyclization alone does not provide sufficient constraint to from a rigid structure, and additional crosslinks are required, such as the 1,4 diazapan-2-one gamma turn mimetic advocated by Ma et al.

Therefore, the claimed invention was within the ordinary skill in the art to make and use at the time the claimed invention was made and was as a whole, *prima facie* obvious.

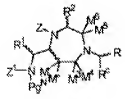
***Maintained Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 113, 119, 120, 121, 124, 126,134,135, 137, 138 and 140 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 113 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships concern the definitions of $M^4$,$R^C$, R and Z. Commensurate with the structure from the claim below:



(a) In section (ii) of claim 113, $M^4$ = M', it is not clear how this is possible and still be a 1,4 diazapan-2-one since $M^4$ being M' may be interpreted as a bicyclic structure.

(b) $R^C$ is selected from the group consisting of $CH_2R$, which if R is H, the side chain of the amino acid glycine set forth in the structure it is not clear what structure is chemically possible since H is monovalent.

(c) Z is selected from the group consisting of $CH_2R$ and C(O)R and suffers similar issues as $R^C$.

(d) Further compounding the confusion, the antecedent basis for R is ambiguous. R is set in the structure at a particular location (ca. 4 O' clock) and is also defined as an amino acid side chain. It is not clear if the R in the definition for Z and $R^c$ refer to the R of the structure or an amino acid side chain, the latter of which may imply a bicyclic or even tricyclic structure.

As currently written, the metes and bounds of the claims are unascertainable. Therefore, claim 113 and all dependent claims are rejected under 35 USC 112, second paragraph.

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Please note that the above rejection has been modified from the original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

*Response to Arguments*

In the remarks entered 10/20/2009, applicant argues the claim is clear to the skilled addressee.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

With regard to item (a) above, on p 12-13 of the remarks applicant contends that $M^4$ = M' means $M^4$ is defined in the same manner as M' (i.e. selected from group consisting of hydrogen, $C_1$ to $C_4$ alkyl, chloro and $C_1$ to $C_4$ alkoxy). This is not persuasive because, the claim may be interpreted in more than one way: as a bicyclic

structure as described in the rejection above or indeed as $M^4$ is selected from the elected from group consisting of hydrogen, $C_1$ to $C_4$ alkyl, chloro and $C_1$ to $C_4$ alkoxy as urged by applicant, therein rendering the metes and bounds of the claim unascertainable.

In this vein, it is noted that the features upon which applicant relies (i.e., $M^4$ is selected from the elected from group consisting of hydrogen, $C_1$ to $C_4$ alkyl, chloro and $C_1$ to $C_4$ alkoxy) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

With regard to item (b) above, on p 13 of the remarks applicant urges that if R is H (the side chain of glycine) implies is $R^C$ $CH_2$-H (methyl). In this regard it is noted the claim does not recite the orientation of $CH_2R$, which may be simply remedied by the addition of a bond thereto (-$CH_2R$).

With regard to item (c), on p 13 of the remarks applicant urges that if R is H (the side chain of glycine) implies is Z $CH_2$-H (methyl) or C(O)H (formyl). In this regard it is noted the claim does not recite the orientation of $CH_2R$ and C(O)R, which may be simply remedied by the addition of a bond thereto (-$CH_2R$ and -C(O)R).

With regard to item (d), on p 14 of the remarks applicant urges that R in Z and $R^c$ means Z and $R^c$ are each defined in the same manner for R in the text (i.e. amino acid side chain groups that may be the same or different). This is not persuasive because, the claim may be interpreted in as many as three ways: as a bicyclic or tricyclic structure as described in the rejection above or indeed as each of $R^c$ and Z being

amino acid side chain groups that may be the same or different as urged by applicant, rendering the metes and bounds of the claim unacertainable.

In this vein, it is noted that the features upon which applicant relies (i.e., Z and $R^c$ being amino acid side chain groups that may be the same or different) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In accordance with MPEP 2173.02: If the language of the claim is such that a person of ordinary skill in the art could not interpret the metes and bounds of the claim so as to understand how to avoid infringement, a rejection of the claim under 35 U.S.C. 112, second paragraph, would be appropriate. See *Morton Int 'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470, 28 USPQ2d 1190, 1195 (Fed. Cir. 1993).

***New Claim Objections***

Claim 113 line 13 is objected to because of the following informalities: $Z^1$ is set forth in the figure, yet the text of the claim refers to Z' (prime). Applicant should be consistent. Appropriate correction is required.

Claim 136 needs a period.

***Specification***

The disclosure is objected to because of the following informalities:

(a) The continuing data should (i.e. 371 data) should appear as the first paragraph in the specification or on an ADS.

(b) A brief description of the drawings is missing.

(c) In the specification, the Greek letters have appear as squares on at least pp 14,15,26 and 32. To properly appreciate the subject matter, which is drawn to gamma turns, beta bends, etc. the correct symbol is necessary. The foregoing page list should not to be deemed exhaustive, however as there may be other missing symbols well.

Applicant is requested to carefully review the specification for the necessary changes, pointing out 35 USC 112 first paragraph support if necessary.

Appropriate correction is required.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER M. GROSS whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571 272 0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

/ Christopher S. F. Low /
Supervisory Patent Examiner, Art Unit 1639